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Technological research in the development of a cosmetic product for acne correction during and after retinoid treatment

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Abstract: *acne is a common dermatological problem significantly affecting patients' quality of life. Retinoids are among the effective treatments, known for their pronounced therapeutic effect. However, prolonged retinoid use is accompanied by side effects such as dryness, redness, irritation, peeling skin, and increased sensitivity to external factors. Cosmetic products with various actions are widely used to minimize these negative manifestations but often only partially compensate for therapy side effects. Therefore, developing a cosmetic product that comprehensively addresses negative skin reactions during and after retinoid treatment remains relevant. Our goal was to investigate the influence of pharmaceutical factors on quality and effectiveness indicators of a cosmetic product in the form of an emulgel for home skincare during and after retinoid acne treatment. An optimal cosmetic product formulation, specifically an emulgel combining emulsion and gel properties, was selected to provide effective moisturizing, nourishment, and skin barrier protection. The study of cosmetic product samples revealed that all tested samples exhibited satisfactory organoleptic properties, with a pH range of 6,73 to 7,11. According to the homogeneity and dispersity analysis, the least stable and most heterogeneous were samples 5 and 9, which demonstrated a diluted structure, significant gaps between particles, and signs of potential phase separation. Evaluation of colloidal stability showed that all tested samples were stable. However, thermodynamic stability testing revealed separation in samples 5 and 6. The best results for spreadability were observed in samples 2, 4, and 8, which showed good distribution ability and effective application during testing. 9 batches of the emulgel were produced, incorporating selected excipients and active ingredients, including plant oils, hydrophilic moisturizers, antioxidants, vitamins, and anti-inflammatory components promoting skin regeneration and reducing irritation. Samples underwent evaluations for organoleptic characteristics, pH, thermostability, colloidal stability, homogeneity, and dispersibility via microscopy. Emulsion type identification was conducted using dye staining. Three batches exhibited satisfactory pharmaceutical-technological properties: batch 2 with 0.5% guar gum solution, batch 4 with 1% sodium alginate solution, and batch 8 with 0.5% high molecular weight sodium hyaluronate solution. Further studies are planned to investigate the consumer characteristics of the selected cosmetic cream samples in order to choose the optimal emulgel composition for home care during retinoid treatment.*

Keywords: Acne Vulgaris; Cosmetics; Skin Cream; Retinoids; Dermatology; technological research, pharmaceutical factors, emulgel.

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Introduction

The research topic's relevance stems from acne's prevalence among adolescents and adults and the need for effective skin care during and after retinoid treatment. Despite proven retinoid effectiveness, their use results in dryness, redness, irritation, peeling, and increased skin sensitivity, significantly discomforting patients and requiring additional skin care products. Existing cosmetic products often inadequately address the comprehensive needs of retinoid-treated skin. Hence, there is a need for multifunctional cosmetic products that moisturize, soothe, regenerate, protect, and enhance skin barrier functions simultaneously [1-5].

Aim

The aim of our work was to conduct technological research in the development of the composition and production technology of an emulgel designed to correct the side effects of retinoid therapy.

Materials and methods

Special attention was given to choosing the cosmetic product formulation – specifically, emulgel – as optimal due to combining gel and emulsion structures, providing deep penetration of active ingredients, prolonged action, and restoration of skin's lipid layer [5-8].

To moisturize the skin, ingredients such as urea, high-molecular-weight sodium hyaluronate, and sodium alginate were used, which retain moisture in the epidermis and promote prolonged hydration. High-molecular-weight sodium hyaluronate, being a natural structural element of the skin, helps maintain moisture levels and enhances skin elasticity and firmness. Urea acts as a natural moisturizer, preventing transepidermal water loss, while sodium alginate creates a protective film on the skin that retains moisture. For skin regeneration, D-panthenol is used, which penetrates into the deeper layers of the epidermis and converts into pantothenic acid, stimulating cell regeneration and the healing of micro-damage. Aloe extract is known for its anti-inflammatory, moisturizing, and soothing properties, making it effective in healing irritated skin. Pomegranate extract, rich in antioxidants, helps protect the skin from oxidative stress and stimulates its renewal. To reduce irritation, plant oils such as rosehip, sweet almond, and avocado oils were introduced. Rosehip oil contains a high concentration of essential fatty acids that help restore the skin's barrier function and reduce flaking. Almond oil also has emollient properties and helps decrease skin sensitivity, while avocado oil, rich in vitamins and antioxidants, provides intensive nourishment and protection. Vitamin E and medicinal plant extracts were used as antioxidants. Vitamin E is a powerful antioxidant that helps combat free radicals, which accelerate skin aging. Vanilla hydrolate adds not only a pleasant fragrance but also provides additional skin-soothing effects [9-11].

Results and Discussion

The creation of a combined product with multifunctional effects – namely anti-inflammatory, regenerative, moisturizing, and softening – is highly important and relevant. This is because consumers seek to minimize the number of skincare products used at home while still achieving long-lasting and high-quality cosmetic effects. A literature review revealed that there is a limited number of acne treatment products with such complex formulations; most usually contain only one or two active pharmaceutical ingredients (APIs).

The pharmaceutical-technological research focused on selecting gel-forming agents. Three different gelling agents were chosen based on literature and usage recommendations. These substances were also introduced in different concentrations to better assess their impact on the quality indicators of the cosmetic product [11]. The composition of the studied samples is shown in Table 1.

The hot emulsification method was used in the preparation of these samples [9-13]. The resulting series were subjected to organoleptic characteristics testing, according to which the following results were obtained.

Series 1, 2, 3: a thick cream with a dense texture, mustard-colored, easy to apply, has a sticky feel, provides a moisturizing sensation. Has a pleasant fresh aroma. *Series 4, 5*, and *6* have a loose, delicate consistency, light-yellow in color, and moderately oily. They are easy to apply and distribute, possess excellent moisturizing properties, and feature a pleasant,

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Table 1– Recipe for emulgel samples for acne correction in home care

Ingredient	Mass, g / Sample number								
	1	2	3	4	5	6	7	8	9
Rosehip oil	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0
Sweet almond oil	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0
Avocado oil	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0
Pomegranate extract	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5
Aloe extract	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5
Vitamin E	0,3	0,3	0,3	0,3	0,3	0,3	0,3	0,3	0,3
D-panthenol	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5
Urea	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0	3,0
Kamaben	0,3	0,3	0,3	0,3	0,3	0,3	0,3	0,3	0,3
Montanov 68	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5	1,5
Guar gum	0,3	0,15	0,075	–	–	–	–	–	–
Sodium alginate	–	–	–	0,3	0,15	0,075	–	–	–
Sodium hyaluronate (high molecular weight)	–	–	–	–	–	–	0,3	0,15	0,075
Vanilla hydrolate	11,4	11,4	11,4	11,4	11,4	11,4	11,4	11,4	11,4

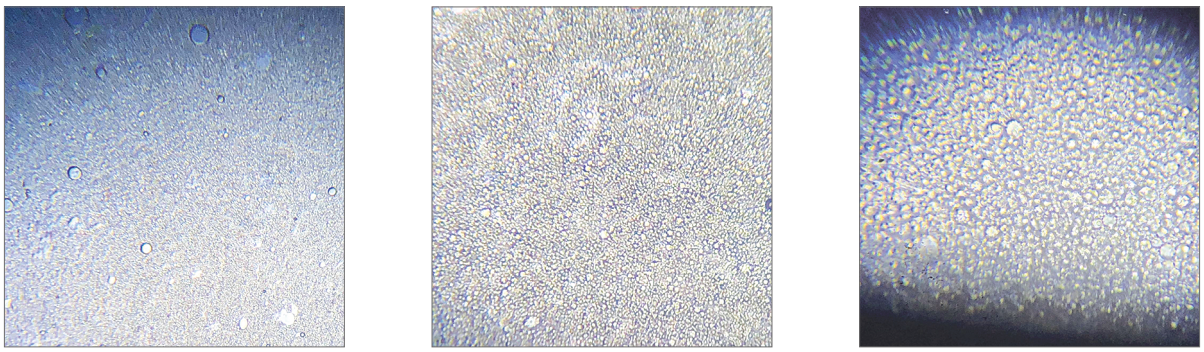
light, fresh scent. *Series 7, 8*, and *9* exhibit an airy, creamy texture, are light-yellow in color, and have outstanding moisturizing properties. They are very easy to apply and distribute, moderately oily, and carry subtle notes of a fresh fragrance.

The next stage of our research was the determination of pH using a pH meter. During the study, it was found that the pH values ranged from 6.73 to 7.11. These results fall within the acceptable range for cosmetic products that are safe for application to the skin and mucous membranes and comply with the requirements of the State Pharmacopoeia of Ukraine [6, 14-15].

Subsequent research involved determining the homogeneity and dispersion of these emulgel using microscopy with a Levenhuk Rainbow 2L NG Amethyst microscope. Samples were examined at three different magnifications: x4, x10, and x40. Additionally, studies were performed to determine the emulsion type through staining. For this purpose, the water-soluble dye methylene blue was used. The obtained results are presented in the figures below [5-6, 14].

Figure 1.1 presents Series 1 of the cosmetic product under investigation.

The photographs show that the sample is homogeneous, with an even distribution of the



x 4 x 10 x 40

Figure 1.1 – Photograph of cosmetic product series 1 under different magnifications.

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oil phase. At magnifications of "×10" and "×40", a finely dispersed structure with uniformly sized particles can be observed.

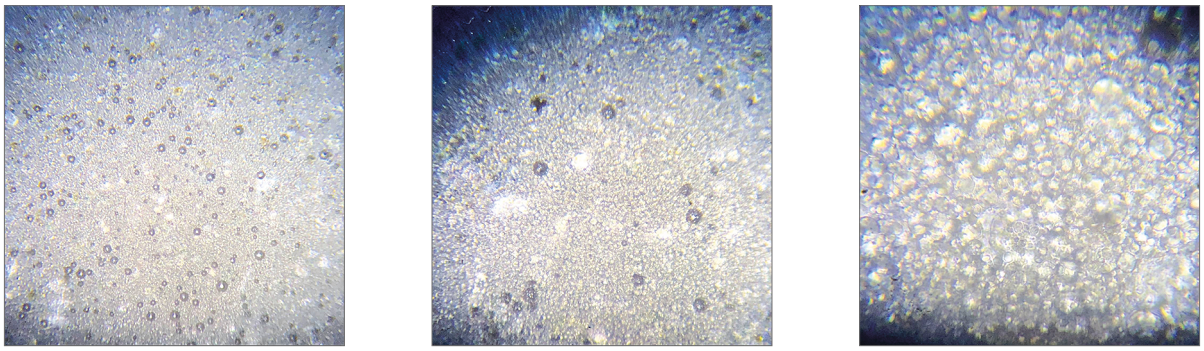
The results of the study of the homogeneity of series 2 are shown in Fig. 1.2.

From the presented drawings of the studied cosmetic product series 2, it is clear that this sample is dense, and you can also observe single inclusions of air bubbles.

The study of the homogeneity and dispersion of series 3 is shown in Fig. 1.3.

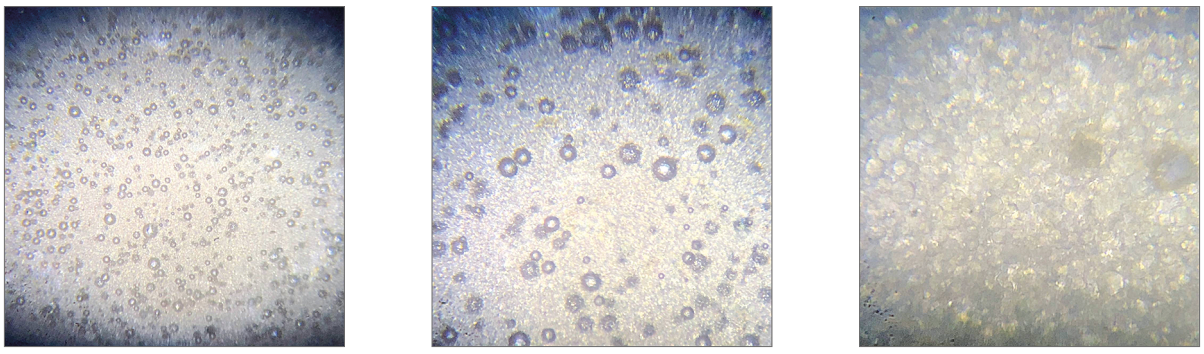
Examining the micrographs of series 3, we found that the obtained sample is dense with an unevenly distributed oil phase. At a magnification of "x40" it is clearly visible that the oil inclusions on the surface are heterogeneous and significantly different in size, and at "x4" and "x10" there are many air bubbles.

The results of the study of series 4 are shown in Fig. 1.4. The studied series is dense in structure, however, in the visible field, there are inclusions of oil droplets of different sizes, which are more



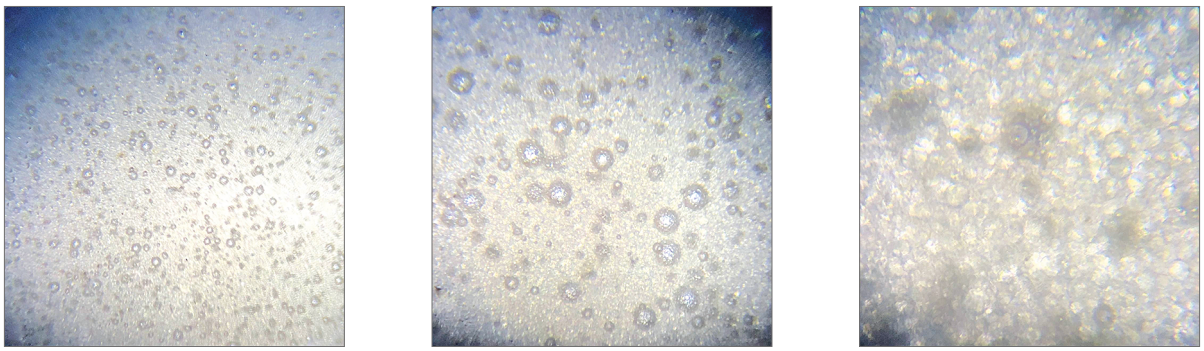
x 4 x 10 x 40

Figure 1.2 – Photograph of cosmetic product series 2 under different magnifications



x 4 x 10 x 40

Figure 1.3 – Photograph of cosmetic product series 3 under different magnifications



x 4 x 10 x 40

Figure 1.4 – Photograph of cosmetic product series 4 under different magnifications

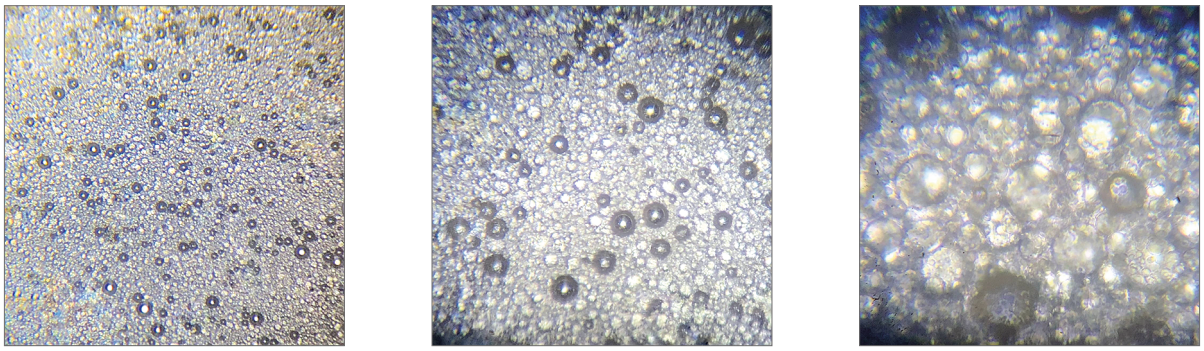
ISSN 2786-6661
eISSN 2786-667X

clearly visible at a magnification of "x10", and there is also a certain number of air bubbles. At a magnification of "x40", the structure is dense and homogeneous.

When studying the homogeneity of series 5, the results are shown in Fig. 1.5. From which it can be seen that the cosmetic has a loose structure with noticeable gaps between the particles, which are coarsely dispersed, which may indicate the instability of the emulsion. At a magnification of "x40", significant differences in the size of the oil droplets are observed, which are large in size.

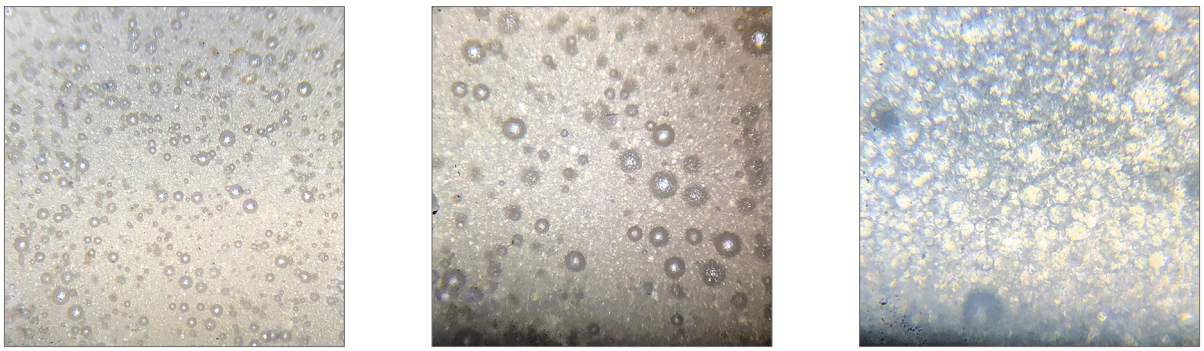
The images in Fig. 1.6 show series 6 of the studied cosmetic product. We can observe that this product, at a magnification of “x40”, has a homogeneous structure with a large number of visible oil inclusions of various sizes, as well as air bubbles.

Figure 1.7. shows the results of the study of series 7. Analyzing the data, we can conclude that this product has a dense structure, but a certain



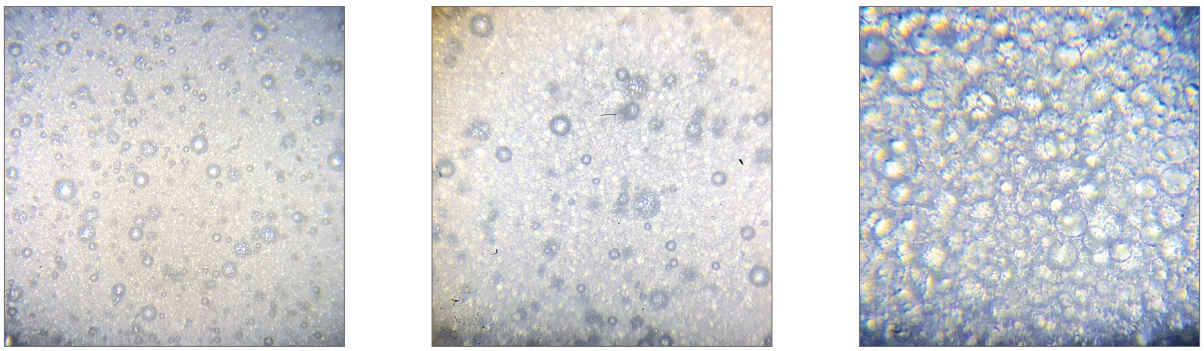
x 4 x 10 x 40

Figure 1.5 – Photograph of cosmetic product series 5 under different magnifications



x 4 x 10 x 40

Figure 1.6 – Photograph of cosmetic product series 6 under different magnifications



x 4 x 10 x 40

Figure 1.7 – Photograph of cosmetic product series 7 under different magnifications

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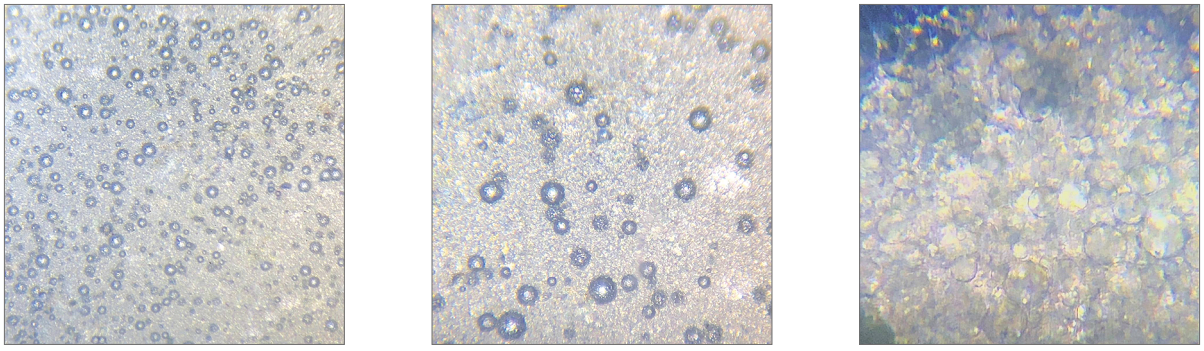
number of air bubbles are observed. The photo shows that the CK has a uniform distribution of the oil phase, which is clearly visible at a magnification of "x40".

The results of the study of series 8 are shown in Fig. 1.8.

The cosmetic product of series 8 is homogeneous and dense in structure, which is clearly visible at a magnification of "x10". There is a certain number of bubbles present, which may indicate a loose structure of the sample.

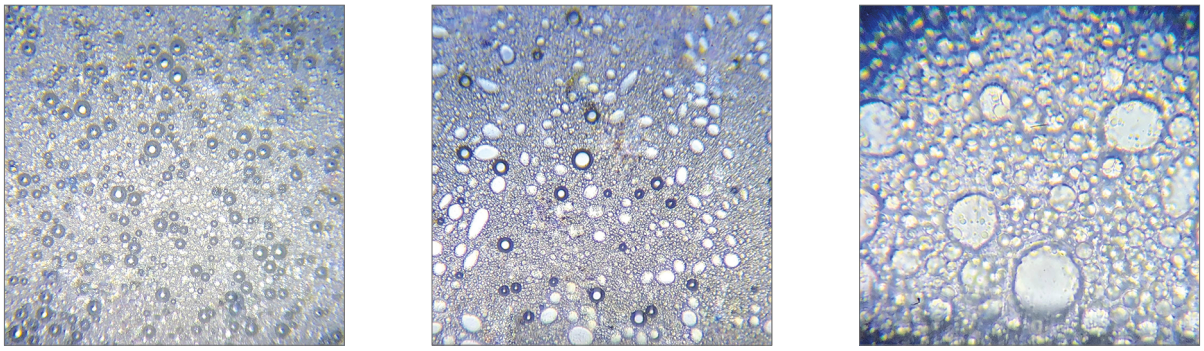
The results of the study for series 9 are shown in Fig. 1.9. This sample is characterized by a heterogeneous, dispersed structure and an uneven distribution of the oil phase. At different magnifications, polydispersity and gaps between particles are evident. At magnifications of ×10 and ×40, oil droplets of varying sizes and numerous air bubbles are visible.

Based on microscopic examination, series 5 and 9 were found to be the least stable and heterogeneous, characterized by a loose



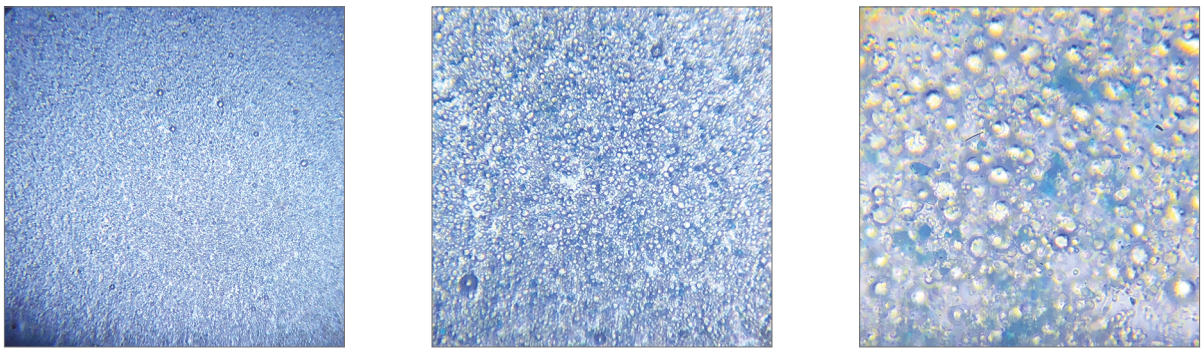
x 4 x 10 x 40

Figure 1.8 – Photograph of cosmetic product series 8 under different magnifications



x 4 x 10 x 40

Figure 1.9 – Photograph of cosmetic product series 9 under different magnifications



x 4 x 10 x 40

Figure 1.10 – Photograph of colored cosmetic product series 4 under different magnifications

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structure, significant gaps between particles, and signs of possible stratification.

To determine the type of emulsion forming the basis of the cosmetic cream, the staining method with the water-soluble dye methylene blue was selected. An aqueous solution of the dye was mixed with a drop of the studied sample and examined under a microscope at different magnifications. The studies revealed that all samples were oil-in-water (o/w) emulsions, in which the aqueous phase was presented as a gel [9].

An example of the research results from one of the series, specifically series 4, is shown in Figure 1.10.

On the presented Fig. 1.10., it is clearly visible that the studied sample is an oil-in-water emulsion, with the field colored blue and transparent oil droplets present against its background.

Our further research focused on determining thermal stability and colloidal stability, which are important indicators of cosmetic product quality. These parameters indicate stability under adverse temperature conditions, which in turn affects the quality and shelf life of creams. To assess thermal stability, the test samples were kept at elevated and reduced temperatures for a specified period of time. Colloidal stability was studied by centrifugation at 6000 rpm for 5 minutes. When evaluating emulsion and emulgel systems, this indicator is crucial, as it reflects the absence of phase separation under shaking conditions [6, 14].

Analyzing the colloidal stability results, it was determined that none of the series underwent separation; however, foam formed on the surface of sample 5. In the thermal stability study, separation occurred in samples 5 and 6. Summarizing both thermal stability and colloidal stability results, it was established that samples 1, 2, 3, 4, 7, 8, and 9 were stable concerning these parameters.

The next study involved determining spreadability, during which the following parameters were evaluated: spreading area, ease of application, rapid absorption, absence of residue, and non-stickiness. The test sample was applied onto the skin at a speed of 10 cm/s in an amount of 0.2 g, after which the coverage area was assessed using filter paper by analyzing the size of the stain left on it [16]. Upon analyzing the obtained results, the best outcomes were achieved with batches 2, 4, and 8, which demonstrated excellent distribution and application efficiency.

The results of the research on cosmetic cream samples are presented in Table 2.

After comparing and analyzing the pharmacotechnological research results, series 2,

Table 2. – The results of the research on cosmetic cream samples

	Sample number				
	No. 1	**No. 2**	**No. 3**	**No.4**	**No.5**
pH value	6.73±0.02	6.87±0.04	6.86±0.02	6.90±0.03	7.01±0.03
Thermal stability	Stable	Stable	Stable	Stable	Not stable
Colloidal stability	Stable	Stable	Stable	Stable	Stable
Spreadability	22.5x14.5cm	34.0x18.5 cm	31.5x14.5 cm	38.5x21.5 cm	28.0x13.5 cm
Organoleptic and sensory properties	A thick, greasy cream that forms a sticky white spot upon application, with a sensation of stickiness.	A slightly greasy cream with a firm texture that moisturizes upon application and forms a white spot that disappears quickly.	A light, gentle cream that forms a white spot upon application, which is difficult to spread.	A light, greasy cream with a smooth consistency. Upon application, it moisturizes and provides pleasant sensory sensations.	A light greasy cream that moisturizes upon application but is poorly absorbed, forming a white spot.

ISSN 2786-6661
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Indicators	Sample number			
	No.6	No.7	No.8	No. 9
pH value	7.03±0.02	6.92±0.02	7.11±0.01	7.08±0.02
Thermal stability	Not stable	Stable	Stable	Stable
Colloidal stability	Stable	Stable	Stable	Stable
Spreadability	25.0x12 cm	23.5x12 cm	31.0x19 cm	27.0x16 cm
Organoleptic and sensory properties	A fluffy, delicate cream that moisturizes upon application but leaves a white spot that spreads and absorbs poorly.	A greasy cream that provides good moisture upon application, but feels sticky and absorbs poorly, forming a viscous, sticky mass.	A fluffy, delicate cream that moisturizes well upon application and does not leave any spots.	A greasy, delicate, fluffy, and watery cream that moisturizes and nourishes well upon application, leaving a white spot that disappears very quickly.

4, and 8 were selected for further in vivo testing and evaluation of consumer properties.

Conclusions

The effect of gelling agents in different concentrations on the pharmaco-technological properties of a cosmetic cream in the form of an emulgel for the correction of acne on the background of retinoid therapy was studied. In the course of the conducted studies, namely: determination of homogeneity and dispersion by microscopy, investigation of thermal stability and colloidal stability, determination of pH and spreadability, 3 series of cosmetic products were selected, which have satisfactory pharmaco-technological properties. These were series 2, 4, and 8.

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Conflict of interest

The authors declare no conflict of interest.

Consent to publication

All authors have reviewed and consented to manuscript publication.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

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Технологічні дослідження при розробці косметичного засобу для корекції вугревої хвороби під час та після лікування ретиноїдами

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Анотація: *вугрова хвороба є поширеною дерматологічною проблемою, яка значно впливає на якість життя пацієнтів. Одним із ефективних методів лікування є застосування ретиноїдів, які мають виражену терапевтичну дію. Однак тривале використання ретиноїдів супроводжується численними побічними ефектами, такими як сухість, почервоніння, подразнення, лущення шкіри та підвищена чутливість до зовнішніх факторів. Для мінімізації цих негативних проявів широко використовуються косметичні засоби з різною дією, проте вони лише частково компенсують побічні ефекти терапії. Тому актуальним є розроблення косметичного засобу, який би комплексно усував негативні реакції шкіри під час та після лікування ретиноїдами. Нашою метою було дослідження впливу фармацевтичних факторів на деякі показники якості та ефективності косметичного засобу у вигляді емульгелю для домашнього догляду при корекції вугревої хвороби під час та після лікування ретиноїдами. З*

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цією метою було обрано оптимальний склад косметичниго засобу, зокрема форми, яка являє собою емульгелт, який поєднує властивості емульсій та гелів, що забезпечує ефективне зволоження, живлення, та захист бар'єру шкіри. Одержано 9 серій досліджуваного емульгелю до складу якого входить обрані допоміжні та активні інгредієнти, а саме рослинні олії, гідрофільні зволожуючі речовини, антиоксиданти, вітаміни та протизапальні компоненти, які сприятимуть регенерації шкіри та зменшенню її подразнення. Для отрманих зразків проводили дослідження органолептичних характеристик, pH, термостабільності та колоїдної стабільність, однорідність та дисперсність складу за допомогою мікроскопії. Також були проведенні дослідження для визначення типу емульсії методом фарбування на намащуваності. При дослідження зразків косметичних засобів встановлено, що всі зразки мають задовільні органолептичні властивості, pH 6,73 - 7,11. Згідно дослідження однорідності і дисперсності встановлено, що найменш стабільними та неоднорідними є серії 5 та 9, які мають розріджену структуру, значні проміжки між частками та ознаки можливого розшарування. Досліджуючи колоїдну стабільність встановлено, що всі досліджувані зразки були стабільними. При дослідженні термостабільності відбулося розшарування 5 і 6 серії досліджуваних кремів. Найкращі результати при досліджуваності намащуваності були отриманні при застосуванні серій 2, 4 та 8, при дослідженні які показали гарну розподільну здатність та ефективність нанесення. В ході проведених досліджень обрано 3 серії косметичного засобу, які володіють задовільними фармако-технологічними властивостями. Це були зразки емульгелю до складу яких входили; 2 серія із 0,5 % розчином гуарової камеді, 4 серія із 1% розчин альгінат натрію, 8 серія із 0,5 % розчину гіалуронату натрію високомолекулярного. . В подальшому плануються дослідження споживчих характеристик обраних досліджуваних зразків косметичного крему, з метою вибору оптимального складу емульгелю для застосування в домашньому догляді на фоні лікування ретоноїдами.

Ключові слова: вугрова хвороба, косметичний засіб, крем, емульгель, ретиноїди, технологічні дослідження, фармацевтичні фактори.